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Regenerable Radical-Trapping Tellurobistocopherol Antioxidants

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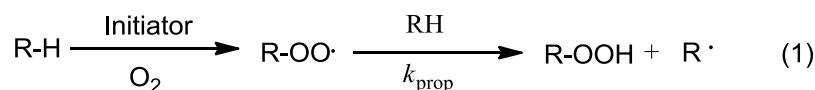
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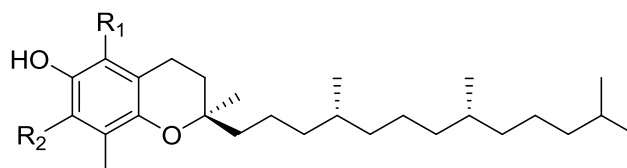
Abstract: Tellurobistocopherols **9-11** were prepared by lithiation of the corresponding bromotocopherols, reaction with tellurium tetrachloride and reductive work-up. Compounds **9-11** quenched linoleic acid-derived peroxy radicals much more efficiently than α -tocopherol in a chlorobenzene/water two-phase system. *N*-Acetylcysteine or tris(2-carboxylethyl)phosphine as co-antioxidants in the aqueous phase could regenerate the tellurobistocopherols and increase their inhibition times. Antioxidant **11** inhibited peroxidation for seven-fold longer than recorded with α -tocopherol. Thiol-consumption in the aqueous phase was monitored and found to be inversely related to the inhibition time.

Oxidative stress is characterized by an imbalance between the production of reactive oxygen species (ROS) and the antioxidant defense systems in favour of the former.¹ ROS is known to target lipids in biological systems and this is generally known as lipid peroxidation, an undesired free radical process whereby organic substances, RH, are oxidized to the corresponding hydroperoxides, ROOH (eq 1).

Vitamin E, the most important lipid-soluble antioxidant in man, offers protection against lipid peroxidation. Briefly, vitamin E (AH) competes with the propagation event and scavenges peroxy radicals, ROO \cdot , by hydrogen-atom transfer (HAT) with a rate $k_{inh} \gg k_{prop}$ (eq 2). The resulting resonance-stabilized radical A \cdot is unable to propagate the reaction.



Vitamin E was first reported by Evans and Bishop in 1922² but its antioxidant properties were revealed by Emerson and co-workers when they showed that it could slow down the autoxidation of fats.³ Vitamin E is a collective name for a family of compounds including four tocopherols and four tocotrienols. Structurally, they are all 6-chromanols. They differ in the number and position of methyl groups in the phenolic part and in the side-chain which is saturated in tocopherols **1-4** and triply unsaturated in the corresponding tocotrienols. In the tocopherol family, α -tocopherol (**1**) is the most reactive compound ($k_{\text{inh}} = 3.2 \times 10^6 \text{ M}^{-1}\text{s}^{-1}$).⁴

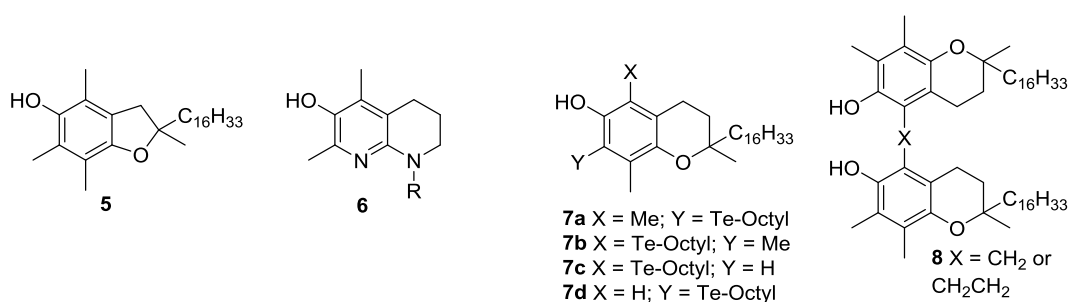


- 1** α -Tocopherol $\text{R}_1 = \text{R}_2 = \text{Me}$
2 β -Tocopherol $\text{R}_1 = \text{Me}; \text{R}_2 = \text{H}$
3 γ -Tocopherol $\text{R}_1 = \text{H}; \text{R}_2 = \text{Me}$
4 δ -Tocopherol $\text{R}_1 = \text{R}_2 = \text{H}$

Considerable efforts have been invested in order to improve the reactivity of **1**. Ingold and coworkers found that compound **5** was a slightly more reactive antioxidant ($k_{\text{inh}} = 4.7 \times 10^6 \text{ M}^{-1}\text{s}^{-1}$)⁵ due to better overlap between the chromane oxygen lone pair and the aromatic ring, resulting in a lower bond dissociation energy, $\text{BDE}_{\text{O-H}}$, of the phenol. More recently, Pratt and coworkers introduced nitrogen into the aromatic ring of α -tocopherol. Thus, strongly electron-donating groups such as amines could be installed to lower the $\text{BDE}_{\text{O-H}}$ while the ionization potential of the compound did not drop below the critical point where electron transfer to dioxygen becomes a problem. Naphthyridinols **6**, representing compounds of this type, were recently found to

efficiently quench peroxy radicals in lipid bilayers.⁶ Suitably positioned chalcogens (Se, S) have also been found to increase the radical trapping activity of phenolic compounds.⁷

Recently, our group showed that alkyltelluro substituted β -, γ - and δ -tocopherols **7a-7d** were at least 10-fold more reactive as radical-trapping agents than their respective parents.⁸



Computational studies on alkyltelluro phenols suggested that oxygen-atom transfer from the peroxy radical to tellurium is a key step in the antioxidant mechanism. The resulting alkoxy radical in the solvent cage can then abstract a hydrogen-atom from the phenolic O-H.⁹ Regeneration of the antioxidant from the phenoxyl radical/telluroxide formed was brought about by thiols (Figure 1). Indeed, the inhibition time for compound **7** was 6.5-fold longer than recorded with α -tocopherol in a two-phase lipid peroxidation system.

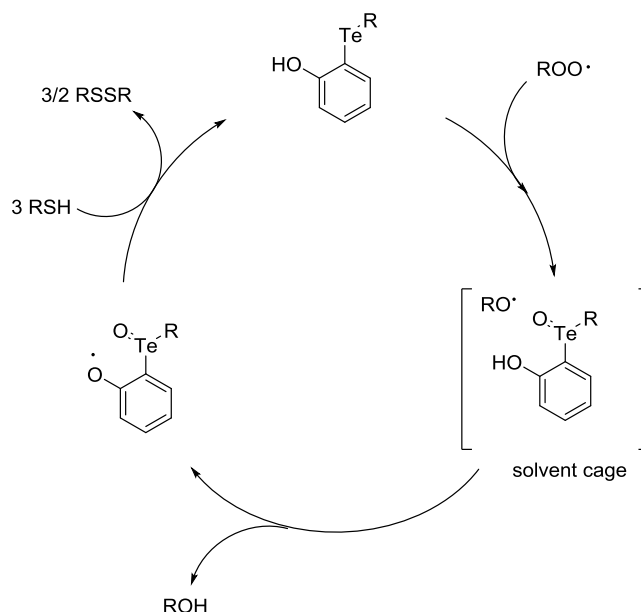
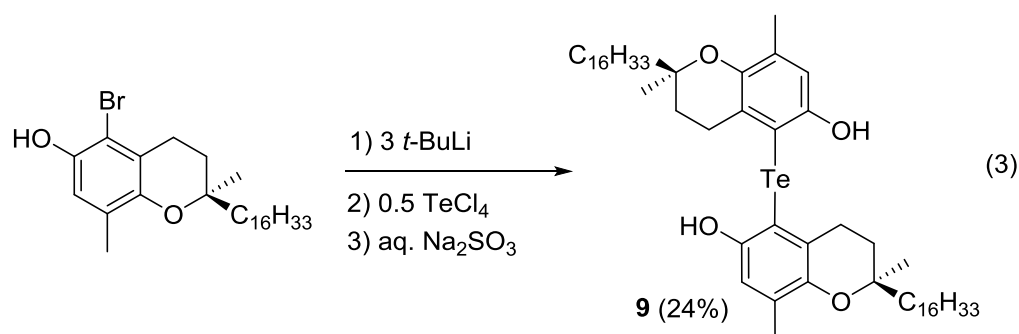


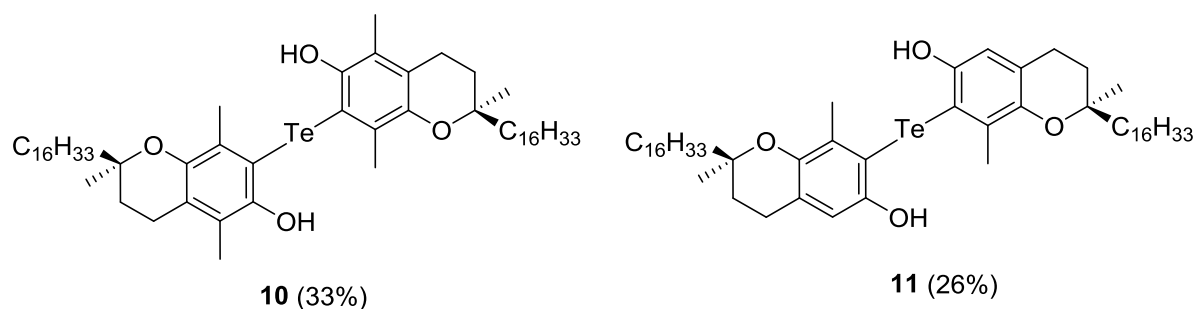
Figure 1. Proposed catalytic mechanism for quenching of peroxy radicals by 2-(alkyltelluro)phenols in the presence of thiols.

It occurred to us that it may be possible to benefit even more from the unusual reactivity of the heteroatom. The idea that emerged was to link two molecules of a tocopherol to tellurium. Surprisingly, only very few compounds of this kind are reported in the literature. They include the methano- and ethano dimers **8**.¹⁰ To the best of our knowledge, dimers linked together by a chalcogen are as yet unknown.

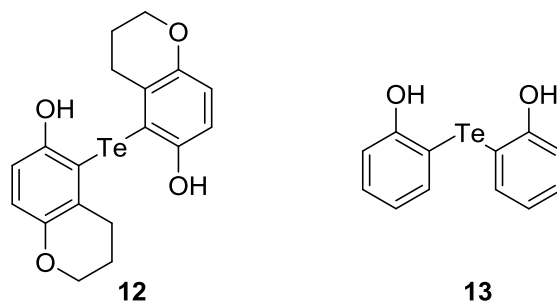
Synthesis: Symmetrical diorganyl tellurides can be obtained in high yields by copper-induced detelluration of the corresponding diorganyl ditellurides.¹¹ This procedure was tried for the preparation of tellurobistocopherol **9**. Although the ditelluride required was conveniently obtained from 5-bromo- δ -tocopherol by dilithiation, Te-insertion into the C-Li bond and air-oxidation, extrusion of tellurium was unsuccessful. Instead, we were pleased to find that a similar strategy, using TeCl₄ in place of elemental tellurium, provided compound **9** in low yield after reductive work-up (eq 3).



In a similar fashion, 7-bromo- β -tocopherol and 7-bromo- δ -tocopherol provided the corresponding tellurobistocopherols **10** and **11** in 33% and 26% yield, respectively.



Curious to study the effects of the phytyl chain, the methyl groups and the benzannulated cyclic ether on antioxidant capacity, compounds **12** and **13** were prepared using a similar procedure.



Evaluation: To determine the radical-trapping capacity and regenerability, all tellurobisphenolic antioxidants were evaluated in a two-phase lipid peroxidation system reminiscent of a biological membrane.¹² Briefly, azobis(2,4-dimethylvaleronitrile) (AMVN) was added as an initiator to chlorobenzene at 42°C containing the antioxidant and linoleic acid as the oxidizable substrate. The aqueous phase contained *N*-acetylcysteine (NAC) or tris(2-carboxylethyl)phosphine (TCEP) which could serve as co-antioxidants and continuously regenerate the

antioxidants in the lipid phase. The chlorobenzene phase was assayed by HPLC every 20 minutes and the concentration of conjugated diene, formed by peroxidation of linoleic acid, was determined by HPLC with UV-detection at 234 nm. Initially, lipid peroxidation is efficiently inhibited by the antioxidant and the rate of conjugated diene formation, R_{inh} , is low. After some time, when the antioxidant is all consumed, the R -value increases considerably to a value corresponding to uninhibited peroxidation. This point is referred to as the inhibition time, T_{inh} , of the antioxidant. Our reference compound, α -tocopherol, at 40 μ M could inhibit peroxidation efficiently (R_{inh} = ca. 25 μ M/h) for ca. 100 min in the presence of aqueous phase NAC or TCEP (Figure 1 and Table 1). The similar T_{inh} - and R_{inh} -values recorded in the absence of the co-antioxidant show that α -tocopherol is not regenerable under the conditions of the two-phase model.

In the absence of NAC/TCEP, all organotellurium antioxidants tested quenched peroxy radicals at least (R_{inh} = 7 – 25 μ M/h), as efficiently as **1**. For compounds **9-11** the T_{inh} -values (165-214 min) were significantly longer than recorded for α -tocopherol.

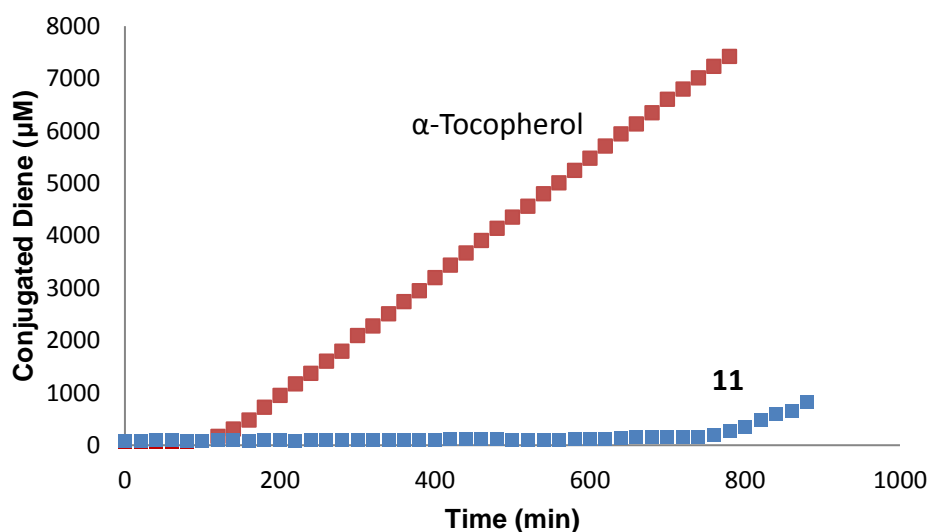


Figure 2. Peroxidation traces (conjugated diene concentration vs time) recorded using compound **11** and α -tocopherol as antioxidants in chlorobenzene and NAC (1 mM) in

the aqueous phase.

When NAC (1 mM) was present in the aqueous phase, the R_{inh} -values were significantly lower for all compounds ($R_{\text{inh}} = 1 - 4 \mu\text{M/h}$) and the T_{inh} -values longer (Table 1). 7,7'-Tellurobis- δ -tocopherol (**11**) inhibited peroxidation for 742 min or 7.6-fold longer than recorded for **11** (Figure 2). This is the longest inhibition time we have ever recorded in the two-phase model. Removal of the phytol chain and the

Table 1. Inhibited Rates of Conjugated Diene Formation (R_{inh}) and Inhibition Times (T_{inh}) in the Presence and Absence of NAC (1.0 mM) or TCEP (0.5 mM) in the Two-phase Model

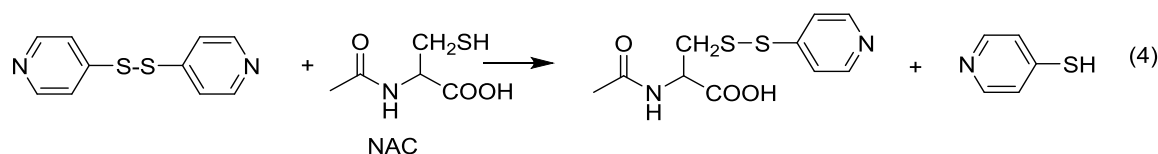
Antioxidants (40 μM)	With NAC		With TCEP		Without NAC/TCEP	
	$R_{\text{inh}}^{\text{a}}$ ($\mu\text{M/h}$)	$T_{\text{inh}}^{\text{b}}$ (min)	$R_{\text{inh}}^{\text{a}}$ ($\mu\text{M/h}$)	$T_{\text{inh}}^{\text{b}}$ (min)	$R_{\text{inh}}^{\text{a}}$ ($\mu\text{M/h}$)	$T_{\text{inh}}^{\text{b}}$ (min)
9	1 ± 1	634 ± 9	2 ± 0	451 ± 9	8	170
10	2 ± 0	653 ± 12	2 ± 1	510 ± 5	7	165
11	4 ± 1	742 ± 13	2 ± 0	507 ± 8	21	214
12	1 ± 1	544 ± 4	2 ± 1	208 ± 10	25	92
13	2 ± 1	365 ± 6	3 ± 1	125 ± 13	11	49
α -Tocopherol	25 ± 1	97 ± 15	21 ± 2	123 ± 7	28	109

^aRate of peroxidation during the inhibited phase (uninhibited rate ca. $479 \mu\text{M/h}$). Errors correspond to \pm SD for triplicates. ^bInhibited phase of peroxidation. Reactions were monitored for 880 min. Errors correspond to \pm SD for triplicates.

2,2',8,8' methyls caused a drop in the inhibition time (compound **12**; $T_{\text{inh}} = 544$ min),

which continued upon further simplification of the structure (compound **13**; $T_{\text{inh}} = 365$ min). We speculate that this is a lipophilicity effect or the result of an increasing $\text{BDE}_{\text{O-H}}$ (*vide infra*).

When TCEP (0.5 mM) was used as a co-antioxidant, similarly low R_{inh} -values were recorded as with NAC (Table 1). Whereas the inhibition times were generally shorter, the similar trend was seen when the compounds were arranged according to falling T_{inh} . We were also curious to see how quickly NAC was consumed during a normal peroxidation experiment. Following a recently described procedure,¹³ the aqueous phase was sampled every 30 minutes and the thiol was allowed to react with bis-4-pyridyl disulfide. The concentration of pyridine-4-thiol formed (eq 4), as determined by UV-spectroscopy at 324 nm, was used for monitoring the disappearance of NAC with time.



For α -tocopherol, the rate of NAC-consumption ($33 \mu\text{M/h}$) was low and essentially the same as recorded in control experiments (nothing but NAC in the two-phase system or NAC + linoleic acid + AMVN; Table 2). When a telluride antioxidant was present, the NAC was consumed more quickly. In the presence of tellurobistocopherols **9-11**, $119 - 131 \mu\text{M/h}$ of the thiol was consumed. The rate increased to 150 and $164 \mu\text{M/h}$, respectively, with compounds **12** and **13**.

Table 2. NAC-Consumption in the Aqueous Phase during Peroxidation Inhibited by Telluriobisphenol Antioxidants

Antioxidant (40 μ M)	Rate of NAC-Consumption (μ M/h) ^a
9	131 \pm 4
10	125 \pm 10
11	119 \pm 13
12	150 \pm 10
13	164 \pm 4
α -Tocopherol	33 \pm 4
^b —	37 \pm 8
^c —	27 \pm 5

^aErrors correspond to \pm SD for triplicates. ^bLinoleic acid and AMVN in the chlorobenzene and NAC in the aqueous phase. ^cNothing in the chlorobenzene and NAC in the aqueous phase.

Thus, the rate of thiol consumption is inversely related to the T_{inh} recorded in the two-phase model. Extrapolation in the NAC-concentration vs time plots to find the time where the aqueous phase was depleted of NAC, showed that this always fell short of the corresponding T_{inh} . It therefore seems that the availability of aqueous-phase NAC is a limiting factor for the inhibition time.

In an attempt to see if the turnover number of catalyst **11** could be increased, the concentration was lowered from the standard 40 μ M to 30, 20, 10 and 5 μ M. As shown in Figure 3, this was not the case. When the concentration was lowered, the T_{inh} was accordingly reduced. A similar trend was seen with TCEP.

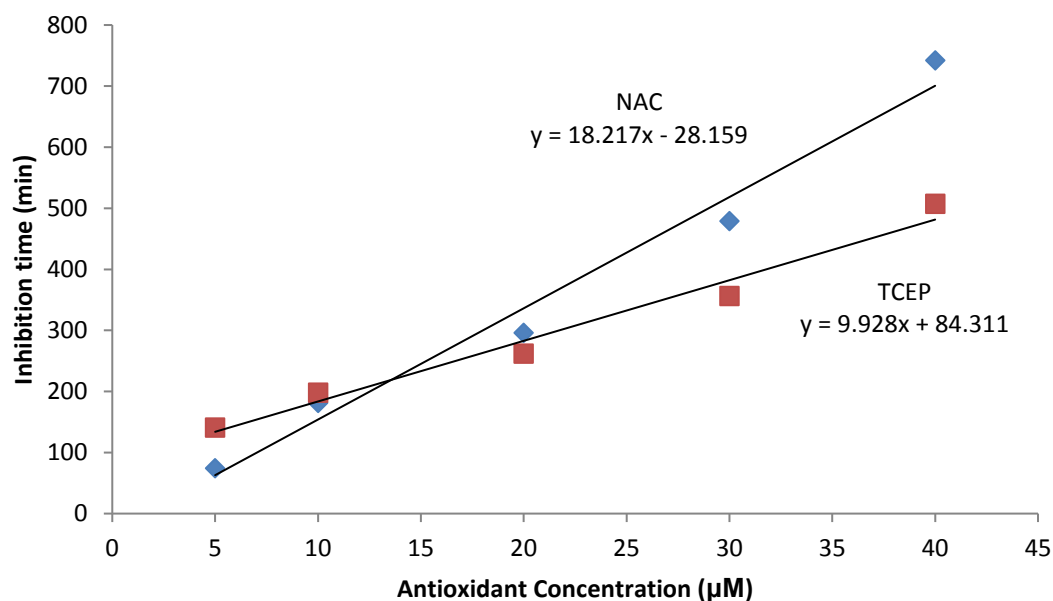


Figure 3. Inhibition times recorded for **11** at different concentrations in the presence of NAC (1.0 mM) or TCEP (0.5 mM).

Concluding Remarks

As observed previously with the “monomeric” tocopherol derivatives **7**, the “dimeric” tellurobistocopherols **9-11** showed considerable antioxidant capacity also in the absence of a co-antioxidant. This may be because the heteroatom is sterically protected. Otherwise, residual amounts of linoleic acid hydroperoxide tend to oxidize the telluride antioxidant to the corresponding telluroxide, which is considerably less reactive towards peroxy radicals.

In the presence of NAC as a co-antioxidant, T_{inh} -values for the “dimers” **9-11** were always longer but never close to twice as long as recorded for the corresponding “monomers” **7a-7d**.^{8b} The largest improvement, +38%, was seen with δ -tocopherol derivative **9** (634 min instead of 458 min for the corresponding monomer **7c**). For compounds **10** (653 min instead of 591 min for **7a**) and **11** (742 min instead of 630 min for **7d**) the increase in T_{inh} was only modest. On the other hand, diaryl

tellurides are chemically more robust than alkyl aryl tellurides. Some time ago we probed the stabilizing capacity of a series of electron-rich diaryl tellurides in polymeric materials.¹⁴ As determined by thermogravimetric analysis many of the compounds were stable at least up to 210° C. Diaryl tellurides as well as alkyl aryl tellurides are easily oxidized to the corresponding telluroxides. In case the system is depleted in reducing agents, there is a risk that the alkyl aryl telluroxide (but not the diaryl telluroxide) may decompose via a telluroxide elimination reaction.¹⁵

The reactivity of the tellurobistocopherols did not change much upon removal of the phytyl chain, the 2,2',8,8'-methyls and the benzannulated cyclic ether. However, a noteworthy drop in the T_{inh} was recorded for compounds **12** and **13**. This could be a lipophilicity effect. Highly lipophilic antioxidants would distribute almost exclusively into the lipid phase and give a maximal antioxidant protection there. Removal of the benzannulated cyclic ether and any methyl groups flanking the aromatic OH would also be expected to cause an increase in the BDE_{O-H} (electron donating substituents here are known to weaken the O-H bond). This would increase leakage of chain-propagating alkoxy radicals from the solvent cage into the bulk of the solution (Figure 1). Whenever this happens, 2 equivalents of thiol are wasted in order to regenerate the catalyst. In fact, such an increase in the rate of thiol consumption was observed for compounds **12** and **13**.

Experimental Section

¹H and ¹³C NMR spectra were recorded on 400 MHz (¹H: 399.97 MHz; ¹³C 100.58 MHz) and 500 MHz (¹H: 499.93 MHz; ¹³C: 125.70 MHz) spectrometers, using the residual solvent peaks of CDCl₃ (¹H: δ 7.26; ¹³C: δ 77.0) as an indirect reference to TMS. ¹²⁵Te NMR spectra were recorded on a 400 MHz spectrometer (¹²⁵Te: 126.19 MHz) using Ph₂Te₂ (423 ppm) as external standard. The melting points are uncorrected.

Flash column chromatography was performed using silica gel (0.04 – 0.06 mm). Tetrahydrofuran was dried in a solvent purification system by passing it through an activated alumina column. 5-Bromo- δ -tocopherol,^{8b} 7-bromo- δ -tocopherol^{8b} and 7-bromo- β -tocopherol^{8b} and 6-bromochromane¹⁶ were prepared according to literature procedures.

General procedure: Synthesis of tellurobisphenols

To a solution of the appropriate 2-bromophenol derivate (1.0 eq.) in anhydrous THF (10 mL) at -78 °C under nitrogen, *tert*-butyl lithium (1.7 M in pentane, 3.0 eq.) was added. After stirring for 2 hours at -78 °C, tellurium tetrachloride (0.5 eq.) was added and the solution was allowed to stir for overnight at ambient temperature. After addition of Na₂SO₃ (aq., 20 mL) and extraction with diethyl ether (25 mL x 3), the organic layer was dried over magnesium sulfate, filtered and evaporated under reduced pressure. The residue was purified by column chromatography (pentane/ethyl acetate = 90:10) to give the title compound.

5,5'-Tellurobis- δ -tocopherol (9). 5-Bromo- δ -tocopherol (964 mg, 2.0 mmol), *tert*-butyl lithium (1.7 M in pentane, 3.5 mL, 6.0 mmol) and tellurium tetrachloride (269 mg, 1.0 mmol) were reacted according to the general procedure to give the title compound as a yellow oil (225 mg, 24%). ¹H NMR (400 MHz, CDCl₃): δ 6.71 (s, 2H), 6.33 (s, 2H), 2.82 (m, 4H), 2.14 (s, 6H), 1.78 (m, 4H), 1.08-1.58 (several peaks, 48H), 0.87-0.91 (several peaks, 24H). ¹³C NMR (100 MHz, CDCl₃): δ 150.9, 146.3, 130.4, 125.5, 114.5, 102.0, 75.2, 39.7, 39.4, 37.5, 37.4, 37.3, 32.8, 32.7, 32.2, 28.7, 28.0, 24.8, 24.4, 23.7, 22.7, 22.6, 21.0, 19.8, 19.6, 16.3. ¹²⁵Te NMR (126 MHz, CDCl₃): δ -3. HRMS (TOF MS EI⁺) *m/z* calcd for C₅₄H₉₀O₄Te [M]⁺: 932.5901. Found: 932.5928.

7,7'-Tellurobis- β -tocopherol (10). 7-Bromo- β -tocopherol (496 mg, 1.0 mmol), *tert*-butyl lithium (1.7 M in pentane, 1.8 mL, 3.0 mmol) and tellurium tetrachloride (134 mg, 0.5 mmol) were reacted according to the general procedure to give the title compound as a yellow oil (158 mg, 33%). ^1H NMR (400 MHz, CDCl_3): δ 5.73 (s, 2H), 2.62 (t, J = 6.4 Hz, 4H), 2.42 (s, 6H), 2.12 (s, 6H), 1.77 (m, 4H), 1.01-1.56 (several peaks, 48H), 0.83-0.88 (several peaks, 24H). ^{13}C NMR (125 MHz, CDCl_3): δ 148.6, 145.5, 129.1, 123.1, 119.1, 105.3, 75.0, 39.8, 39.4, 37.4, 37.3, 32.8, 32.7, 31.4, 28.0, 24.8, 24.4, 23.7, 22.7, 22.6, 21.2, 21.1, 20.9, 19.8, 19.6, 12.6. ^{125}Te NMR (126 MHz, CDCl_3): δ 33. HRMS (MALDI) m/z calcd for $\text{C}_{56}\text{H}_{94}\text{O}_4\text{Te}$ $[\text{M}]^+$: 960.6214. Found: 960.6217.

7,7'-Tellurobis- δ -tocopherol (11). 7-Bromo- δ -tocopherol (964 mg, 2.0 mmol), *tert*-butyl lithium (1.7 M in pentane, 3.5 mL, 6.0 mmol) and tellurium tetrachloride (269 mg, 1.0 mmol) were reacted according to the general procedure to give the title compound as a yellow oil (238 mg, 26%). ^1H NMR (400 MHz, CDCl_3): δ 6.65 (s, 2H), 6.61 (s, 2H), 2.68 (m, 4H), 2.52 (s, 6H), 1.75 (m, 4H), 1.06-1.60 (several peaks, 48H), 0.88-0.92 (several peaks, 24H). ^{13}C NMR (100 MHz, CDCl_3): δ 150.5, 145.4, 132.5, 124.0, 111.5, 105.9, 76.0, 40.1, 39.4, 37.4, 37.3, 32.8, 32.7, 31.2, 28.0, 24.8, 24.4, 24.0, 22.7, 22.6, 22.5, 22.4, 21.0, 19.7, 19.6. ^{125}Te NMR (126 MHz, CDCl_3): δ 49. HRMS (TOF MS ESI) m/z calcd for $\text{C}_{54}\text{H}_{90}\text{O}_4\text{Te}$ $[\text{M}+\text{Na}]^+$: 955.5794. Found: 955.5801.

6-Chromanol. To a mixture of magnesium turnings (248 mg, 10.2 mmol) and iodine (90 mg, 0.35 mmol) in THF (4 mL) under nitrogen was added a solution of 6-bromochromane (378 mg, 1.8 mmol) in anhydrous THF (2 mL). After heating at 60 °C for 20 min, a solution of 6-bromochromane (1.14 g, 5.3 mmol) in anhydrous THF (6 mL) was added dropwise over a period of 50 min at 30 °C. The Grignard reagent was

transferred to a solution of trimethyl borate (0.79 mL, 7.1 mmol) in anhydrous THF (4 mL) at -10 °C over a period of 1 hour. The reaction mixture was allowed to stir for 30 min prior to hydrolysis with HCl (2 M, 12 mL) and extraction with diethyl ether (10 mL). The organic phase was washed with water (10 mL x 2) and then transferred to a two-neck round-bottomed flask. To the solution, peracetic acid (1.2 mL, 39% in acetic acid) was added dropwise at 0°C under nitrogen. After stirring at ambient temperature for 3 hours, the reaction mixture was quenched with NaHSO₃ (10% aq., 30 mL) and extracted with diethyl ether (30 mL x 3). The organic layer was dried over magnesium sulfate, filtered and evaporated under reduced pressure. The residue was purified by column chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a white solid. ¹H NMR (400 MHz, CDCl₃): 6.67 (d, *J* = 8.8 Hz, 1H), 6.57 (dd, *J* = 2.8, 8.8 Hz, 1H), 6.53 (d, *J* = 2.8 Hz, 1H), 4.40 (s, 1H), 4.13 (t, *J* = 4.8 Hz, 2H), 2.74 (d, *J* = 6.4 Hz, 2H), 1.98 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): 148.9, 148.8, 123.0, 117.3, 115.8, 114.3, 66.3, 25.0, 22.4. ¹H and ¹³C spectra were in accord with the literature.¹⁷

5-Bromo-6-chromanol. To a solution of 6-chromanol (651 mg, 4.3 mmol) in dichloromethane (50 mL), a solution of tetrabutylammonium tribromide (2.1 g, 4.3 mmol) in dichloromethane (50 mL) was added dropwise. After stirring for one hour, the solution was evaporated and the residue was purified by column chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a white solid (685 mg, 70%). ¹H NMR (400 MHz, CDCl₃): δ 6.82 (d, *J* = 6.8 Hz, 1H), 6.73 (d, *J* = 6.8 Hz, 1H), 5.16 (s, 1H), 4.08 (m, 2H), 2.73 (t, *J* = 5.6 Hz, 2H), 2.02 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 149.5, 146.1, 122.1, 116.8, 113.9, 112.6, 65.8, 26.3, 22.3. ¹H and ¹³C spectra were in accord with the literature.¹⁷

5,5'-Tellurobis-6-chromanol (12). 5-Bromo-6-chromanol (458 mg, 2.0 mmol),

tert-butyl lithium (1.7 M in pentane, 3.5 mL, 6.0 mmol) and tellurium tetrachloride (269 mg, 1.0 mmol) were reacted according to the general procedure to give the title compound as a red solid (135 mg, 32%). Mp = 158-160 °C. ¹H NMR (500 MHz, CDCl₃): δ 6.79 (d, *J* = 9.0 Hz, 2H), 6.73 (d, *J* = 9.0 Hz, 2H), 6.23 (s, 2H), 4.03 (t, *J* = 5.0 Hz, 4H), 2.80 (t, *J* = 7.0 Hz, 4H), 1.98 (m, 4H). ¹³C NMR (125 MHz, CDCl₃): δ 151.9, 149.1, 127.5, 120.0, 113.0, 106.4, 65.7, 31.2, 23.2. ¹²⁵Te NMR (126 MHz, CDCl₃) δ 216. HRMS (TOF MS EI⁺) *m/z* calcd for C₁₈H₁₈O₄Te [M]⁺: 428.0267. Found: 428.0272.

2,2'-Tellurobisphenol (13). 2-Bromophenol (692 mg, 4.0 mmol), *tert*-butyl lithium (1.7 M in pentane, 7.0 mL, 12.0 mmol) and tellurium tetrachloride (538 mg, 2.0 mmol) were reacted according to the general procedure to give the title compound as a pale yellow solid (270 mg, 44%). ¹H NMR (500 MHz, CDCl₃): δ 7.52 (dd, *J* = 2.0, 8.0 Hz, 2H), 7.26 (m, 2H), 6.96 (dd, *J* = 1.5, 8.5 Hz, 2H), 6.78 (m, 2H), 5.92 (s, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 156.9, 139.5, 131.3, 122.2, 114.2, 102.2. ¹²⁵Te NMR (126 MHz, CDCl₃) δ 285. The ¹H spectrum was in accord with the literature.¹⁸

HPLC Peroxidation Assay. The experimental setup for the two-phase lipid peroxidation model for determination of *R*_{inh} and *T*_{inh} has been recently described.¹² The values for *R*_{inh} and *T*_{inh} in the presence of NAC and TCEP are reported as means ± SD based on triplicates. The initial concentration of linoleic acid hydroperoxide was ca. 175 μM at the beginning of each experiment.

NAC-consumption Assay. The experimental setup for determination of the rate of NAC-consumption in the two-phase lipid peroxidation model was recently described.¹³ The values reported are means ± SD based on triplicates.

ASSOCIATED CONTENT

Supporting Information

^1H , ^{13}C and ^{125}Te NMR data for all new compounds prepared. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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Graphical Abstract

